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(54) **Bone regeneration membrane**

Membran für Knochenregenerierung

Membrane pour la régénération osseuse

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(73) Proprietor: **Synthes AG, Chur**
CH-7002 Chur (CH)

(72) Inventors:
- **Gogolewski, Sylwester**
  7492 Alvaneu-Dorf (CH)
- **Perren, Stephan M.**
  CH-7260 Davos (CH)
- **Meinig, Richard M.**
  Colorado Springs, Co 80906 (US)

(74) Representative: **Lusuardi, Werther Giovanni, Dr.**
Dr. Lusuardi AG,
Kreuzbühlstrasse 8
CH-8008 Zürich (CH)

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Description

1. Field of the invention

This invention relates to a bone regeneration membrane containing resorbable or degradable polymeric and/or polymeric-ceramic material according to the preamble of claim 1.

Diaphyseal bone loss results from high-energy trauma, infection, or resection performed for skeletal neoplasia. The numerous treatment modalities attest to the difficulty in obtaining reliable and satisfactory reconstitution of skeletal long bone defects. Methods for treating diaphyseal bone defects include: autologous cancellous or cortical bone grafts, autologous vascularized bone transplants and grafts, xenogenic bone grafts, allogenic bone grafts, hydroxyapatite and/or tricalcium phosphate ceramics implants, coral, natural polymers like collagen, synthetic polymers like polyethylene and polyglycolide, osteoinductive proteins such as bone morphogenetic protein, and bone transport techniques.
All these methods have failed in producing predictable reconstruction of cortico-cancellous bone loss from diaphyseal segment of the human skeleton.

2. Description of the Prior Art

Various proposals have been made for the application of membranes containing resorbable or degradable polymeric material for bone regeneration purposes.

From an article of Magnusson, Batich and Collins, published in the J. Periodontol., Jan. 1988 pp.1-5, it is known to utilize very thin membranes of unspecified porosity and consisting of low-molecular weight polylactic acid for the regeneration of the dental cementum.

It is also known from Dahlin, Linde, Gottlow and Nyman (Plastic and Reconstructive Surgery, May 1988, pp.672 - 676) to use a porous polytetrafluoroethylene membrane for healing bone in the jaw.

It is further known from Farso-Nielsen, Karring and Gogolewski (IADR General Session, March 7-11, 1990, Cincinnati, Ohio) to use elastic biodegradable polyurethane membranes of unspecified structure for healing bone defects in rabbits.

From Warrer, Karring, Nyman and Gogolewski (paper submitted to J.Periodontol. 1990) it is further known that the use of membranes consisting of unspecified polylactic acid or polyurethane polymers failed to produce regeneration of periodontal defects.

With all these prior art membranes of largely unspecified structure and chemistry clinical results are rather unpredictable and vary from author to author.

3. Summary of the Invention

The present invention is intended to remedy these drawbacks. It solves the problem of how to design a membrane containing resorbable or degradable polymeric and/or polymeric-ceramic material having a well-defined structure and chemistry which - when properly fashioned and applied - will promote spontaneous human bone regeneration as well as improve the efficacy of adjunctive bone conductive and inductive substances.

The invention solves the problem with a membrane comprising the features of claim 1 and a use of the membrane comprising the features of claim 24.

Briefly described the invention comprises a bone regeneration membrane containing resorbable or degradable polymeric and/or polymeric-ceramic material having a glass transition temperature in the range of -30°C to +200°C, the membrane having micropores therein. Preferably the glass transition temperature of said polymeric and/or polymeric-ceramic material is in the range of +10° to +90°C and most preferably between +30 to +70°C.

Glass transition temperature has surprisingly turned out to be of great importance, since application of membranes made of low glass transition temperature polymeric materials to bone defects have resulted in undesired external callus formation.

Chemically the membrane is prepared from highly purified resorbable and/or degradable polymers and/or polymer-ceramics such as polyhydroxyacids, polysaccharides, polyamines, polyaminoacids, polyorthoesters, polyanhydrides, collagen or composites thereof with tricalcium phosphate and/or hydroxyapatite, whereby preferably at least 90 weight percent of the material has a molecular weight in the range of 5'000 to 1'000'000, preferably in the range of 25'000 to 150'000 and most preferably in the range of 30'000 to 70'000.

In terms of molecular weight distribution, (or polydispersity) the polymeric and/or polymeric-ceramic material should have a polydispersity in the range of 1,2 to 100,0, preferably in the range of 1,9 to 2,5.

Structurally the membrane is generally thin and preferably microporous.
The thickness of the membrane can be controlled to meet structural demands of the proposed implantation site, but should range between 0,05 to 5,0 mm, preferably between 0,2 to 3,0 mm and most preferably between 0,4 to 1,5 mm.
The specific pore size, shape and structure to be selected for a certain application is variable to a large extent, whereby at least 90 percent of the micropores present in the polymeric material should have a diameter below 500 µm, preferably in the range of 0,01 to 50,0 µm and most preferably in the range of 0,1 to 5 µm. What is essential is that the micropores are permeable for nutritional fluids. Therefore the micropores within the membrane should be preferably interconnected to allow liquids penetration and circulation.

A membrane having the structural and chemical features according to the invention exhibits a resorption rate in vivo in the range from 2 weeks to 1 year and longer. The resorption rate can be adjusted to a desired value (e.g. to over one year for the treatment of large defects) by altering the polymer molecular weight, the polymer chain orientation and crystallinity, physical structure,

chemical composition, presence and extent of voids, additives and so on.

The membranes can be used in a planar form, but generally are prefashioned or modified intraoperatively by the surgeon to conform to a curved surface, preferably a rectilinear surface. Most suitable are membranes with an adaptable surface, preferably a cylindrical surface, which most preferably is of tubular (circular cylinder) form.

In a preferred embodiment the membrane according to the invention is shaped in tubular form, preferably with a longitudinal slit to allow variability of the tubular diameter over a wide range. The diameter of the tubular membrane should match the dimensions of the bone to be treated, e.g. 4.0 to 50.0 mm for tibia reconstructions. A thin membrane of e.g. 0.1 mm thickness can also be rolled up either pre- or intraoperatively to form a final tubular implant with a wall thickness of e.g. 3.1 mm.

In a preferred embodiment the overlapping, intersected tubular membrane according to the invention provides semi-occlusive fits at the two extremities of the tube for better external adaptation to the cortical bone ends and/or internal adaptation within medullary canals of long or tubular bones.

It is of importance that the internal membrane tube to be inserted into an intramedullary canal, is formed on a mandrel which has an external diameter at least 1.1 to 3.0 times bigger than the diameter of the intramedullary canal. The external membrane tube should be formed on a mandrel which has an external diameter which is at least 1.1 to 3.0 times smaller than the external diameter of the bone. Due to its "shape memory" the tubular membrane can be easily placed and fit on the bone to be treated.

If two tubular membranes are used (an external over the cortical bone ends and a internal within the medullary canal) they can either be used with or without spacers between the two tubular membranes. The two membranes can either be supplied preoperatively as a single unit (with interconnecting structures) or can be assembled intraoperatively by the surgeon. Accordingly one membrane is rolled in a tubular fashion to obtain a press fit into the medullary canal of both bone fragments, and a second membrane is rolled into a tube to form a semi-occlusive external sleeve, bridging the two bone fragment ends. The space between the two membranes forms a new artificial cortex that can be filled with a variety of therapeutic substances, such as autologous bone, allogenic bone, demineralized bone powder extracts, bone morphogenetic protein isolates, antibiotics, or anti-neoplastic drugs.

The walls of the membranes can either be continuous or intersected longitudinally for better adaptation of the membrane on the bone. If necessary, the space between the inner and outer tubular membranes can be maintained in their relative position by means of spokes, ribs or other corrugated elements attached permanently, or inserted between the membrane tubes upon surgery.

The membrane tube can be used as a complete construction or only as a part of the construction (e.g. a half construction) depending on the bone defect to be treated.

The membranes according to the invention can be used for a variety of applications to span osseous defects that have been conventionally stabilized with an external fixator, intramedullary rod , or systems of plates and screws, of which the most important are listed below:

- as a tissue separator which promotes and protects osseous regeneration;
- for the treatment of osseous defects secondary to trauma, infection, neoplasm, or surgical resection;
- as cortical spacer across bone defects;
- as an osseous activity barrier that confines bone regeneration to desired regions and prevents the formation of synostosis, physeal bars, or ectopic bone;
- as a spacer for skeletal resection, revision arthroplasty, or arthrodesis of human joints;
- as a container for autologous or allogenic graft materials; and
- as a combined bone grafting and/or drug delivery system.

The membrane according to the invention, therefore, offers a novel treatment that reliably promotes osseous healing with and without adjunctive therapies, while posing no toxic risks or requirements for extensive surgery for implantation or removal. The membrane can be preoperatively shaped and adjusted by the surgeon to conform and integrate with a wide range of anatomical defects and locations.

The advantages offered by the invention are mainly the following:

- maintainance of a physical barrier that contains osseous activity of the host bone, while simultaneously protecting this osseous activity from nonosteogenic and interfering cell lines.
- protection of the cortical and medullary canal osteogenic capacity from surrounding soft tissues and inflammatory reactions.

4. Brief Description of the Drawings

The various features of novelty which characterize the invention are pointed out with particularity in the claims annexed to and forming part of this disclosure. For the better understanding of the invention, its operating advantages and specific objects attained by its use, reference should be had to the accompanying drawings, examples and descriptive matter in which are illustrated and described preferred embodiments of the invention.

In the drawings,

Fig. 1 is a simplified perspective view of a membrane in accordance with the invention;

Fig. 2 is a side elevation schematically illustrating the technique for applying a membrane in accordance with the invention;;

Fig. 3 is a side elevation schematically illustrating an application of membranes in the intramedullary canal as well as externally; and

Fig. 4 is an illustration of an application similar to Fig. 3 wherein the space between membranes is filled with autogenic cancellous bone graft.

5. Description of the Preferred Embodiments

The membranes according to the invention can be produced by any technique known to those skilled-in-the-art, e.g. by solvent-casting, extrusion, injection-moulding, vacuum-forming, blowing, spraying, brushing, polymerization, compression-moulding, etc. Two specific examples are given below:

Example I:

Poly(L-lactide) with a viscosity-average molecular weight in the range of 15.000 - 700.000 Daltons were purified twice by dissolution in chloroform followed by precipitation with methanol. Polymers were dried under vacuum to constant weight and kept in a desiccator over molecular sieves. Microporous, resorbable membranes were prepared in the phase-reverse technique. Flat membranes were wetted in polar or nonpolar liquids and preshaped over mandrels of suitable shape, to fit the approximate diameter of the implantation site. The membranes were preshaped to the anatomy of the bone to be covered. Wet membranes rolled up on the mandrels were covered with aluminium foil to protect them against unrolling and placed at 50 - 150°C in the vacuum oven for 0.5 - 6.0 hours.

After removal of the aluminium foil the membrane 1 had the configuration as shown in Fig. 1. Thanks to the longitudinal slit 2 parallel to its central axis 3 and its inherent shape memory it was adaptable in diameter over a large extent to match bone ends of different sizes and diameters.

The membrane produced according to this example had a glass transition temperature of + 50°C.

The pore size of the membrane was in the range of 0.1 to 1.0 µm and its thickness was 1,0 mm.

Viscosity average molecular weight of the polymeric membrane according to this example was 75'000, and its molecular weight distribution was 2,2.

The tubular membranes were used to cover a diaphyseal defect of ten rabbits. Two months after surgery the canal created by the membrane according to this example was filled with osseous tissue.

Example II:

Microporous resorbable membranes were prepared from poly(L-lactide) with a viscosity-average molecular weight of 15'000 to 100'000 Daltons according to the method of manufacture described in Example I.

The membrane produced according to this example had a glass transition temperature of +50°C and showed a porosity in the range of 10 to 50 µm and a thickness of 0,9 mm.

Numerous controlled experiments by the applicants have demonstrated that the novel membranes obtained by the described methods of manufacture promote bone growth in a reliable manner and further improve the efficacy of adjunctive bone conductive and inductive substances.

The membrane obtained by the method according to Example II was sterilized with ethylene oxide and implanted in 15 mature rabbits, to cover mid-diaphyseal defects of 10 mm created in the radius of a limb. An identical, but untreated defect on the other limb served as a control.

Within one week the membrane implants were filled with tissues that progressively differentiated into osseous tissue. By one month, further osseous formation had bridged 40 to 95 % of the defect. New bone was formed within the inner canal of the polymeric membrane tube. In contrast, the control defects were occupied by overlying muscle and soft tissues.

The application of the membranes according to the invention is now further described by having reference to the drawings:

In a first application, shown in Fig. 2, a tubular membrane 1 was pulled over the aligned and correctly positioned extremities 4,5 of a fractured long bone 6 and affixed thereto by means of wires 7,8. Of course the membrane 1 can be affixed to the bone ends 4,5 by a variety of suitable means including external suture, metal or polymer screws, and/or plate and band combinations. The whole assembly was further fixed by means of an external fixator 9.

In a second application, shown in Fig. 3, prior to the fixation of the external membrane 1, a second tubular membrane 11 was previously inserted in the intramedullary canal 12, thereby forming a confined space 13, which as shown in Fig. 4 was filled with autogenic cancellous bone graft 14.

Claims

1. A bone regeneration membrane comprising resorbable or degradable polymeric and/or polymeric-ceramic material, characterized in that

   A) said polymeric material comprises polyhydroxyacids, polysaccharides, polyamines, polyaminoacids, polyorthoesters, polyanhydrides, collagen or composites thereof with tricalcium phosphate and/or hydroxyapatite;

   B) at least 90 weight percent of said polymeric and/or polymeric-ceramic material has a molecular weight in the range of 5'000 to 1'000'000;

C) said polymeric and/or polymeric-ceramic material has a molecular weight distribution in the range of 1,2 to 100,0;

D) the glass transition temperature of said polymeric and/or polymeric-ceramic material is in the range of -30° to + 200°C; and

E) said membrane is provided with micropores.

2. A membrane according to claim 1, characterized in that said glass transition temperature of said polymeric and/or polymeric-ceramic material is in the range of +10° to + 90°C, preferably between +30 to +70°C.

3. A membrane according to claim 1 or 2, characterized in that at least 90 percent of said micropores have a diameter below 500 µm, preferably in the range of 0,01 to 50,0 µm, most preferably in the range of 0,1 to 5 µm.

4. A membrane according to one of the claims 1 to 3, characterized in that said micropores are interconnected.

5. A membrane according to one of the claims 1 to 4, characterized in that at least 99 weight percent of said polymeric and/or polymeric-ceramic material has a molecular weight in the range of 5'000 to 1'000'000.

6. A membrane according to one of the claims 1 to 5, characterized in that it further comprises reinforcement including resorbable and/or degradable fibers.

7. A membrane according to one of the claims 1 to 6, characterized in that it has a thickness of between 0,05 to 5,0 mm, preferably between 0,2 to 3,0 mm, most preferably between 0,4 to 1,5 mm.

8. A membrane according to one of the claims 1 to 7, characterized in that at least 90 weight percent of said polymeric material has a molecular weight in the range of 25'000 to 150'000, preferably in the range of 30'000 to 70'000.

9. A membrane according to one of the claims 1 to 8, characterized in that said polymeric material is highly purified.

10. A membrane according to one of the claims 1 to 9, characterized in that it further contains antibiotic agents.

11. A membrane according to one of the claims 1 to 10, characterized in that it further contains antiosteomyelitis agents.

12. A membrane according to one of the claims 1 to 11, characterized in that it further contains antineoplastic agents.

13. A membrane according to one of the claims 1 to 12, characterized in that it further contains osteoconductive agents of autogenic, allogenic, xenogenic, or synthetic origin.

14. A membrane according to one of the claims 1 to 13, characterized in that it further contains osteoinductive agents of autogenic, allogenic, xenogenic, or synthetic origin.

15. A membrane according to one of the claims 1 to 14, characterized in that it has a curved surface, preferably a rectilinear surface.

16. A membrane according to claim 15, characterized in that said rectilinear surface is an adaptable surface, preferably a cylindrical surface.

17. A membrane according to one of the claims 1 to 16, characterized in that it has a shape memory.

18. A membrane according to one of the claims 1 to 16 characterized in that it is formable into a tubular form, preferably with a longitudinal slit.

19. A membrane according to claim 18, characterized in that it is adapted to form semi-occlusive fits at the two extremities of the tube formed by said membrane for fixation to bones.

20. A membrane according to claim 18, characterized in that it has ends shaped to form semi-occlusive fits over cortical bone ends and within medullary canals of long or tubular bones.

21. A membrane according to claim 18 , characterized in that it comprises a sheet prefashioned into a tubular form.

22. A membrane according to claim 18 , characterized in that it is rolled up to form a multilayer tube.

23. A membrane according to one of the claims 1 to 22, characterized in that said polymeric and/or polymeric-ceramic material has a molecular weight distribution in the range of 1,9 to 2,5.

Patentansprüche

1. Knochenregenerierungsmembran, die resorbierbares oder abbaubares Polymer- und/oder Polymerkeramikmaterial enthält, dadurch gekennzeichnet, daß

A) das Polymermaterial Polyhydroxysäuren, Polysaccharide, Polyamine, Polyaminosäuren, Polyorthoester, Polyanhydride, Kollagen oder Verbundstoffe hiervon mit Trikalziumphosphat und/oder Hydroxyapatit hergestellt umfaßt,

B) wenigstens 90 Gewichtsprozent des Polymer- und/oder Polymerkeramikmaterials ein Molekulargewicht zwischen 5.000 bis 1.000.000 aufweisen,

C) das Polymer- und/oder Polymerkeramikmaterial eine Molekulargewichtsverteilung zwischen 1,2 und 100,0 aufweist,

D) der Einfrierpunkt zwischen -30 °C und +200 °C liegt und

E) die Membran Mikroporen aufweist.

2. Membran gemäß Patentanspruch 1, dadurch gekennzeichnet, daß der Einfrierpunkt des Polymer- und/oder Polymerkeramikmaterials zwischen +10 °C und +90 °C liegt, vorzugsweise zwischen +30 °C und +70 °C.

3. Membran gemäß Patentanspruch 1 oder 2, dadurch gekennzeichnet, daß wenigstens 90 Prozent der Mikroporen einen Durchmesser unter 500 µm aufweisen, vorzugsweise zwischen 0,01 und 50,0 µm, optimal zwischen 0,1 und 5 µm.

4. Membran gemäß einem der Patentansprüche 1 bis 3, dadurch gekennzeichnet, daß die Mikroporen untereinander verbunden sind.

5. Membran gemäß einem der Patentansprüche 1 bis 4, dadurch gekennzeichnet, daß wenigstens 99 Gewichtsprozent des Polymer- und/oder Polymerkeramikmaterials ein Molekulargewicht zwischen 5.000 und 1.000.000 aufweisen.

6. Membran gemäß einem der Patentansprüche 1 bis 5, dadurch gekennzeichnet, daß sie zudem eine Verstärkung mit resorbierbaren und/oder abbaubaren Fasern umfaßt.

7. Membran gemäß einem der Patentansprüche 1 bis 6, dadurch gekennzeichnet, daß sie eine Dicke zwischen 0,05 und 5,0 mm aufweist, vorzugsweise zwischen 0,2 und 3,0 mm, optimal zwischen 0,4 und 1,5 mm.

8. Membran gemäß einem der Patentansprüche 1 bis 7, dadurch gekennzeichnet, daß wenigstens 90 Gewichtsprozent des Polymermaterials ein Molekulargewicht zwischen 25.000 und 150.000 aufweisen, vorzugsweise zwischen 30.000 und 70.000.

9. Membran gemäß einem der Patentansprüche 1 bis 8, dadurch gekennzeichnet, daß das Polymermaterial hochrein ist.

10. Membran gemäß einem der Patentansprüche 1 bis 9, dadurch gekennzeichnet, daß sie zudem antibiotische Wirkstoffe enthält.

11. Membran gemäß einem der Patentansprüche 1 bis 10, dadurch gekennzeichnet, daß sie zudem antiosteomyelitische Wirkstoffe enthält.

12. Membran gemäß einem der Patentansprüche 1 bis 11, dadurch gekennzeichnet, daß sie zudem antineoplastische Wirkstoffe enthält.

13. Membran gemäß einem der Patentansprüche 1 bis 12, dadurch gekennzeichnet, daß sie zudem osteokonduktive Wirkstoffe autogenen, allogenen, xenogenen oder synthetischen Ursprungs enthält.

14. Membran gemäß einem der Patentansprüche 1 bis 13, dadurch gekennzeichnet, daß sie zudem osteoinduktive Wirkstoffe autogenen, allogenen, xenogenen oder synthetischen Ursprungs enthält.

15. Membran gemäß einem der Patentansprüche 1 bis 14, dadurch gekennzeichnet, daß sie eine gewölbte, vorzugsweise eine Regelfläche aufweist.

16. Membran gemäß Patentanspruch 15, dadurch gekennzeichnet, daß es sich bei der Regelfläche um eine anpassungsfähige - vorzugsweise eine zylinderförmige - Fläche handelt.

17. Membran gemäß einem der Patentansprüche 1 bis 16, dadurch gekennzeichnet, daß sie ein Formgedächtnis hat.

18. Membran gemäß einem der Patentansprüche 1 bis 16, dadurch gekennzeichnet, daß sie sich zu einer Röhre - vorzugsweise mit einem Längsschlitz - formen läßt.

19. Membran gemäß Patentanspruch 18, dadurch gekennzeichnet, daß sie angepaßt wird, um halbokklusive Passungen an den beiden Enden der Röhre entstehen zu lassen, die zwecks Befestigung an die Knochen aus dieser Membran gebildet wird.

20. Membran gemäß Patentanspruch 18, dadurch gekennzeichnet, daß ihre Enden so geformt sind, daß sie halbokklusive Passungen über den Kortikalknochen-Enden und im Innern des Knochenmarkkanals langer oder röhrenförmiger Knochen bilden.

21. Membran gemäß Patentanspruch 18, dadurch gekennzeichnet, daß sie eine röhrenförmig vorgeformte Platte enthält.

22. Membran gemäß Patentanspruch 18, dadurch gekennzeichnet, daß sie aufgerollt wird, um eine Mehrschichtröhre zu bilden.

23. Membran gemäß einem der Patentansprüche 1 bis 22, dadurch gekennzeichnet, daß das Polymer- und/oder Polymerkeramikmaterial eine Molekulargewichtsverteilung zwischen 1,9 und 2,5 aufweist.

Revendications

1. Membrane pour la régénération osseuse, comprenant un matériau polymérique et/ou polymérique-céramique pouvant se résorber ou se dégrader, caractérisée en ce que

   A) ledit matériau polymérique comprend des polyhydroxyacides, des polysaccharides, des polyamines, des polyaminoacides, des polyorthoesters, des polyanhydrides, du collagène ou des composites de ceux-ci avec du phosphate tricalcique et/ou de l'hydroxyapatite;
   B) au moins 90 pourcent en poids dudit matériau polymérique et/ou polymérique-céramique présentent un poids moléculaire dans la plage de 5000 à 1000000;
   C) ledit matériau polymérique et/ou polymérique-céramique présente une distribution de poids moléculaire dans la plage de 1,2 à 100,0;
   D) la température de transition vitreuse dudit matériau polymérique et/ou polymérique-céramique est dans la plage de -30° à +200°C; et
   E) ladite membrane est dotée de des micropores.

2. Membrane selon la revendication 1, caractérisée en ce que ladite température de transition vitreuse dudit matériau polymérique et/ou polymérique-céramique est dans la plage de +10° à +90°C, de préférence entre +30 et +70°C.

3. Membrane selon la revendication 1 ou 2, caractérisée en ce que au moins 90 pourcent desdits micropores présentent un diamètre inférieur à 500 µm, de préférence dans la plage de 0,01 à 50,0 µm, mieux encore dans la plage de 0,1 à 5 µm.

4. Membrane selon l'une quelconque des revendications 1 à 3, caractérisée en ce que lesdits micropores sont interconnectés.

5. Membrane selon l'une quelconque des revendications 1 à 4, caractérisée en ce que au moins 99 pourcent en poids dudit matériau polymérique et/ou polymérique-céramique présentent un poids moléculaire dans la plage de 5000 à 1000000.

6. Membrane selon l'une quelconque des revendications 1 à 5, caractérisée en ce qu'elle comprend en outre des renforts comprenant des fibres pouvant se résorber et/ou se dégrader.

7. Membrane selon l'une quelconque des revendications 1 à 6, caractérisée en ce qu'elle présente une épaisseur entre 0,05 et 5,0 mm, de préférence entre 0,2 et 3,0 mm, mieux entre 0,4 et 1,5 mm.

8. Membrane selon l'une quelconque des revendications 1 à 7, caractérisée en ce qu'au moins 90 pourcent en poids dudit matériau polymérique présentent un poids moléculaire dans la plage de 25000 à 150000, de préférence dans la plage de 30000 à 70000.

9. Membrane selon l'une quelconque des revendications 1 à 8, caractérisée en ce que ledit matériau polymérique est hautement purifié.

10. Membrane selon l'une quelconque des revendications 1 à 9, caractérisée en ce qu'elle comprend en outre des agents antibiotiques.

11. Membrane selon l'une quelconque des revendications 1 à 10, caractérisée en ce qu'elle contient en outre des agents antiostéomyélites.

12. Membrane selon l'une quelconque des revendications 1 à 11, caractérisée en ce qu'elle contient en outre des agents antinéoplastiques.

13. Membrane selon l'une quelconque des revendications 1 à 12, caractérisée en ce qu'elle contient en outre des agents ostéoconducteurs d'origine autogène, allogène, xénogène ou synthétique.

14. Membrane selon l'une quelconque des revendications 1 à 13, caractérisée en ce qu'elle contient en outre des agents ostéoinducteurs d'origine autogène, allogène, xénogène ou synthétique.

15. Membrane selon l'une quelconque des revendications 1 à 14, caractérisée en ce qu'elle présente une surface courbe, de préférence une surface réglée.

16. Membrane selon la revendication 15, caractérisée en ce que ladite surface rectiligne est une surface adaptable, de préférence une surface cylindrique.

17. Membrane selon l'une quelconque des revendications 1 à 16, caractérisée en ce qu'elle présente une mémoire de forme.

18. Membrane selon l'une quelconque des revendications 1 à 16, caractérisée en ce qu'elle peut être façonnée en forme tubulaire, de préférence avec une fente longitudinale.

19. Membrane selon la revendication 18, caractérisée en ce qu'elle est adaptée pour former des ajustements semi-occlusifs aux deux extrémités du tube formé par ladite membrane pour la fixation aux os.

20. Membrane selon la revendication 18, caractérisée en ce qu'elle présente des extrémités mises en forme pour former des ajustements semi-occlusifs sur les extrémités des os spongieux et à l'intérieur des canaux médullaires des os tubulaires ou longs.

21. Membrane selon la revendication 18, caractérisée en ce qu'elle comprend une feuille préformée en une forme tubulaire.

22. Membrane selon la revendication 18, caractérisée en ce qu'elle est enroulée pour former un tube multicouches.

23. Membrane selon l'une quelconque des revendications 1 à 22, caractérisée en ce que ledit matériau polymérique et/ou polymérique-céramique présente une distribution de poids moléculaire dans la plage de 1,9 à 2,5.

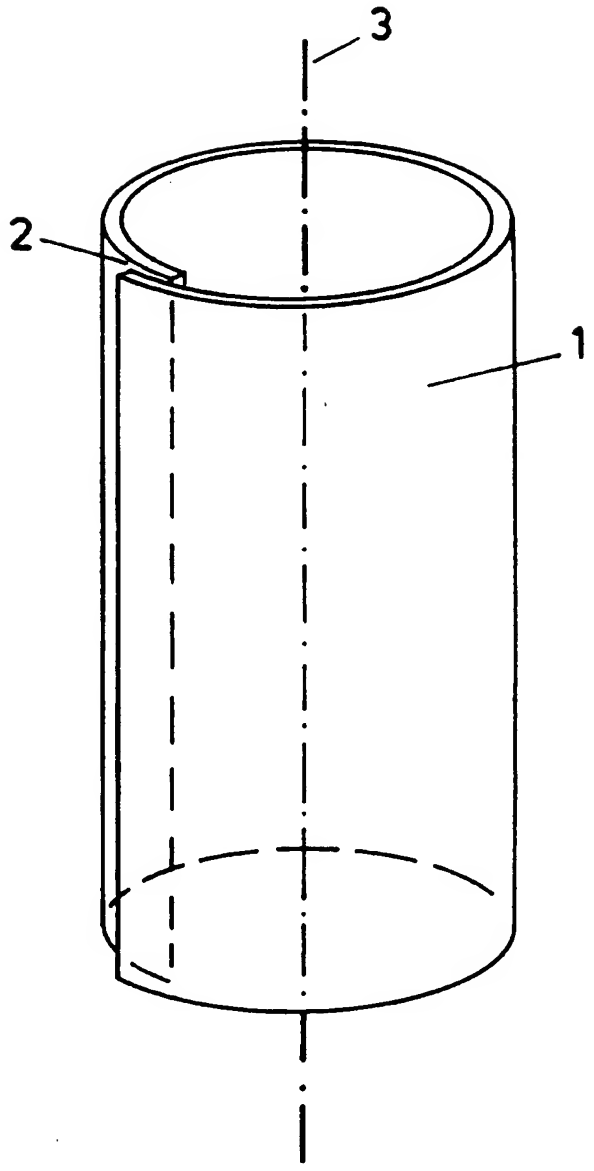

Fig. 1

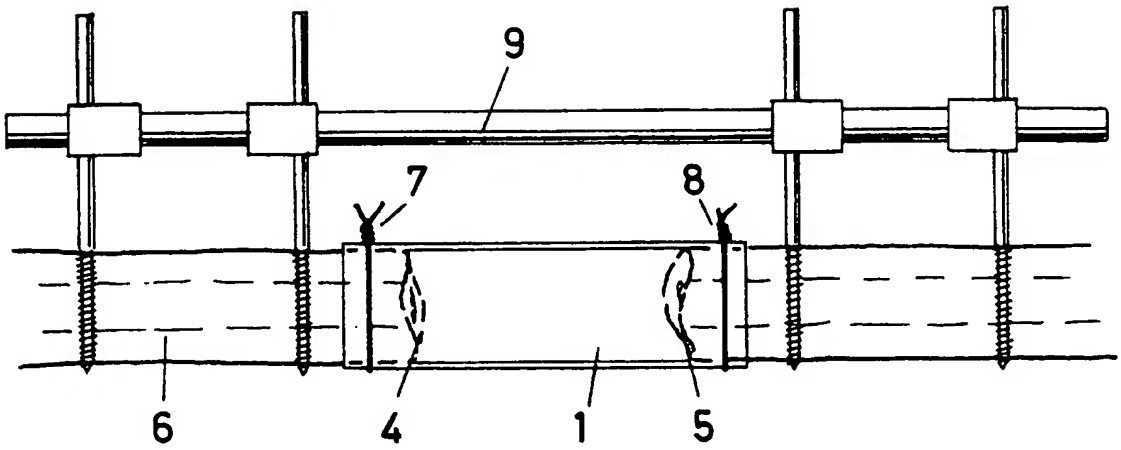

Fig. 2

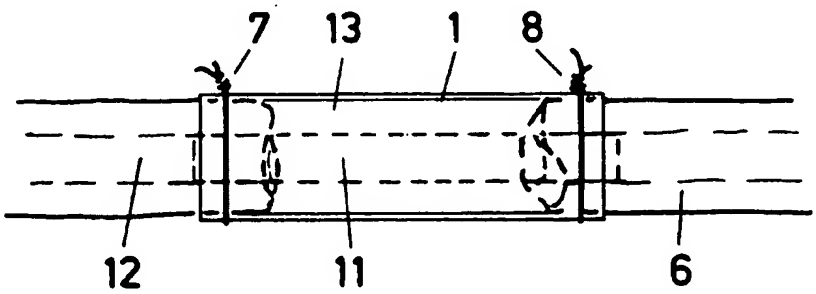

Fig. 3

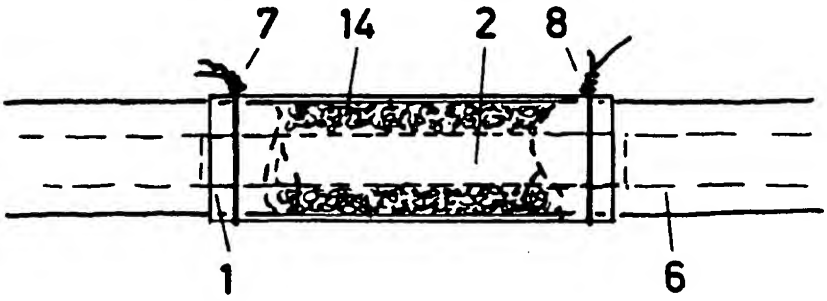

Fig. 4